Complete Summary

GUIDELINE TITLE

Appropriate patient preparation for renal replacement therapy.

BIBLIOGRAPHIC SOURCE(S)

Renal Physicians Association. Appropriate patient preparation for renal replacement therapy. Rockville (MD): Renal Physicians Association; 2002 Oct. 78 p. (Renal Physicians Association Clinical Practice Guideline; no. 3). [252 references]

GUIDELINE STATUS

This is the current release of the guideline.

It is estimated that in light of the rate of production of new evidence, the current clinical practice guideline will require updating in three to five years.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Advanced chronic kidney disease (CKD) stages 4 and 5, with a glomerular filtration rate (GFR) of $\leq$30 mL/min/1.73 m^2 not on renal replacement therapy (dialysis or transplantation)

GUIDELINE CATEGORY

Counseling
Evaluation
Management

Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Endocrinology
Family Practice
Hematology
Internal Medicine
Nephrology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide clinicians with practical guidance for the care of individuals with advanced chronic kidney disease (CKD) not yet requiring renal replacement therapy

TARGET POPULATION

Adult patients 18 years of age and older with advanced chronic kidney disease (CKD) not yet on renal replacement therapy (RRT) who are expected to progress and require renal replacement therapy within 6 to 18 months

Note: This guideline is not intended for use in children and adolescents.

INTERVENTIONS AND PRACTICES CONSIDERED

Management and Risk Assessment

1. Evaluation for anemia, including hemoglobin (Hb) and/or hematocrit (Hct), red blood cell (RBC) indices, reticulocyte count, and iron parameters (e.g., serum iron, total iron binding capacity [TIBC], percent transferrin saturation [TSAT], serum ferritin, test for occult blood in stool).
2. Blood pressure monitoring
3. Serum bicarbonate monitoring for acidosis
4. Serum calcium and phosphorus measurement
5. Immunoreactive parathyroid hormone (iPTH) measurement
6. Nutritional status monitoring, such as body weight, serum albumin, serum total protein, prealbumin, transferrin and total cholesterol, body mass index, skin fold thickness, mid-arm muscle circumference, subjective global assessment
7. 24-hour urine collection for urea nitrogen
8. Measurement of triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and total cholesterol

Treatment

1. Intravenous or oral iron therapy
2. Erythropoietin or erythropoietin analogue
3. Sodium bicarbonate or calcium carbonate
4. Low phosphorus/low protein diet
5. Phosphate binder (calcium-based or non-calcium-based phosphate binder)
6. Vitamin D therapy, such as calcitriol or alfacalcidol
7. Elemental calcium
8. Therapeutic lifestyle modifications
    - Dietary changes
    - Smoking cessation
    - Weight reduction and management
    - Regular or increased physical activity
    - Moderating alcohol consumption
    - Cautious glycemic control
9. Diuretic therapy, including thiazide and/or loop diuretic
10. Angiotensin converting enzyme (ACE) inhibitor
11. Angiotensin II receptor blocker (ARB)
12. Diet assessment, nutritional assessment, and nutritional counseling
13. Statins
14. Fibrates, such as gemfibrozil
15. Nicotinic acid
16. Patient education regarding renal replacement therapy
17. Employment counseling, such as vocational counseling

MAJOR OUTCOMES CONSIDERED

- Prevalence of anemia in patients with advanced chronic kidney disease (CKD) and correlation with renal function
- Risk for and incidence of renal osteodystrophy in patients with advanced CKD and its correlation with metabolic acidosis
- Risk for and incidence of hyperparathyroidism with hypocalcemia and hyperphosphatemia in patients with advanced CKD
- Incidence of vitamin-D deficiency and bone fracture rates in patients with advanced CKD
- Risk for hypertension in patients with advanced CKD
- Risk for malnutrition in advanced CKD and correlation with decline in glomerular filtration rate
- Risk for and prevalence of dyslipidemia in advanced CKD and correlation with atherosclerotic cardiovascular disease
- Level of kidney function (glomerular filtration rate [GFR])
- Mortality
- Quality of life and functional status

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Working Group identified a series of specific questions relevant to the following topics: anemia, bone disease, hypertension, lipid disorders, timing and preparation for renal replacement therapy (RRT), and counseling. For each question, the Duke Evidence-based Practice Center (EPC) staff (on contract to the Renal Physicians Association for development of this guideline and associated measures) developed a literature search strategy of electronic databases, consisting of groups of specific search terms. The comprehensive literature search covered all the available published peer-reviewed literature in English from January 1988 to December 2001. Additional ad hoc searches included articles published through February 2002.

Using detailed inclusion criteria, the Duke physicians screened these articles and identified additional studies from the reference list of included articles.

NUMBER OF SOURCE DOCUMENTS

Anemia

Five hundred and five titles and abstracts were initially screened. Of these, 70 were identified for full-text screening. The Duke Evidence-based Practice Center was unable to obtain a copy of two of these articles. Of the remaining 68, twenty-five were excluded during full-text review for the following reasons: outcomes not reported separately for the pre-end stage renal disease (ESRD) population (n = 1), did not meet the criteria for the pre-ESRD population (n = 3), did not address at least one of the key questions (n = 21). The remaining non-review articles (thirty-two) were abstracted using a standardized form and are summarized in Evidence Table 1 in the companion evidence report.

Bone Disease

Four hundred and seventy-two titles and abstracts were screened (467 from the ECRI database plus five others). One hundred and twenty of these were identified for full-text screening. The Duke Evidence-based Practice Center was unable to obtain copies of five of these articles. Of the remaining 115, 95 were excluded during full-text review for the following reasons: outcomes not reported separately for the pre-ESRD population (n = 4), did not meet the criteria for the pre-ESRD population (n = 31), did not address at least one of the key questions (n = 61). Fourteen articles were included at the full-text screening stage: one of these was a review article; the remaining 13 were abstracted using a standardized form and are summarized in Evidence Table 2 in the companion evidence report.

Hypertension

Two hundred and sixty-two titles and abstracts were initially screened. Of these, 89 were identified for full-text screening. The Duke Evidence-based Practice

Center was unable to obtain copies of six of these articles. Of the remaining 83, 62 were excluded during full-text review for the following reasons: outcomes not reported separately for the pre-ESRD population (n = 1); did not meet the criteria for the pre-ESRD population (n = 11); small case series/single case report (n = 3); did not address at least one of the key questions (n = 47). Twenty-three articles were included at the full-text screening stage: they were abstracted using a standardized form and are summarized in Evidence Table 3 in the companion evidence report.

Nutrition

Seven hundred and ninety-six titles and abstracts were initially screened. Of these, 138 were identified for full-text screening. The Duke Evidence-based Practice Center was unable to obtain copies of 14 of these articles. Of the remaining 124, 83 were excluded during full-text review for the following reasons: outcomes not reported separately for the pre-ESRD population (n = 1), did not meet the criteria for the pre-ESRD population (n = 9), small case series/single case report (n = 2), did not address at least one of the key questions (n = 71). Sixty-five articles were included at the full-text screening stage: 29 of these were review articles; the remaining 36 were abstracted using a standardized form and are summarized in Evidence Table 4 in the companion evidence report.

Dyslipidemias

Five hundred and twenty-two titles and abstracts were screened. Seventy of these were identified for full-text screening. Of these 70 articles, 58 were excluded at the full-text screening stage for the following reasons: outcomes not reported separately for the pre-ESRD population (n = 4), did not meet the criteria for the pre-ESRD population (n = 13), small case series/single case report (n = 2), did not address at least one of the key questions (n = 39). The Duke Evidence-based Practice Center was unable to obtain copies of two articles. Of the 12 articles included at the full-text screening stage, one was a review article; the remaining 11 were abstracted using a standardized form and are summarized in Evidence Table 5 in the companion evidence report.

Timing the Initiation of Renal Replacement Therapy

One hundred and eighty-two titles and abstracts were screened. Of these, 59 were identified for full-text screening. The Duke Evidence-based Practice Center was unable to obtain copies of six of these articles. Of the remaining 53, 30 were excluded during full-text review for the following reasons: did not meet the criteria for the pre-ESRD population (n=3), small case series/single case report (n = 1), or did not address at least one of the key questions (n = 26). In all, a total of 23 articles were abstracted using a standardized form and are summarized in Evidence Table 6 in the companion evidence report.

Counseling and Rehabilitation

Education/Counseling

Twelve studies, described in 15 publications, described the association between education and patient satisfaction, knowledge or outcomes. One report described two separate studies, while several studies were described in more than one report.

Exercise

The Duke Evidence-based Practice Center identified seven studies of physical activity counseling or exercise therapy in the pre-ESRD population. Three of these studies were randomized controlled trials, two were non-randomized concurrent cohort comparisons, and one was an uncontrolled (before/after) prospective single-subject design trial.

Employment Counseling

The Duke Evidence-based Practice Center identified two studies of predialysis programs aimed at maintaining employment, both retrospective studies comparing program participants. One was a controlled study among patients on in-center hemodialysis and the other was an uncontrolled study among patients on home dialysis.

Evaluation (individualized assessment)

The Duke Evidence-based Practice Center found only one study that described the use of individualized clinical assessment. This study is described in the section on "Education" in the companion evidence report.

Encouragement (emotional support)

The Duke Evidence-based Practice Center found no studies describing clinician-delivered encouragement, broadly defined, offered to pre-ESRD patients.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Level of Evidence for Different Types of Studies:

Adapted from Ball C, Sackett D, Phillips B, Haynes B, and Straus S. Levels of evidence and grades of recommendations. Ver 17 Sept 1998. http://www.minervation.com/cebm/docs/levels.html. Accessed 7/28/02.

Therapy/Prevention or Etiology/Harm

- Level 1a: Systematic review (with homogeneity) of randomized controlled trials (RCTs)
- Level 1b: Individual RCT (with narrow confidence interval)
- Level 1c: All or none

- Level 2a: Systematic review (with homogeneity) of cohort studies
- Level 2b: Individual cohort study (including low quality RCT; e.g., <80% follow-up)
- Level 2c: "Outcomes" research
- Level 3a: Systematic review (with homogeneity) of case-control studies
- Level 3b: Individual case-control study
- Level 4: Case-series (and before/after studies and poor quality cohort and case-control studies)
- Level 5: Expert opinion without explicit critical appraisal, or based on psychology, bench research or "first principles."

Prognosis/Natural history

- Level 1a: Systematic review (with homogeneity) of inception cohort studies or a clinical practice guideline validated on a test set
- Level 1b: Individual inception cohort study with at least 80% follow-up
- Level 1c: All or none case series
- Level 2a: Systematic review (with homogeneity) of either retrospective cohort studies or untreated control groups in RCTs
- Level 2b: Retrospective cohort study or follow-up of untreated control patients in an RCT; or clinical practice guideline not validated in test set
- Level 2c: "Outcomes" research
- Level 4: Case-series (and poor quality prognostic cohort studies)
- Level 5: Expert opinion without explicit critical appraisal, or based on psychology, bench research or "first principles."

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Included articles from the literature search were summarized in evidence tables and synopses. The quality of each article was assessed using a standard measure intended to assess design and analysis factors that can reduce bias in clinical studies.

The Duke Evidence-based Practice Center (EPC) staff produced an extensive review of the available published evidence on effective treatment in this population, "Evidence Report: Appropriate Patient Preparation for Renal Replacement Therapy" (see the "Companion Documents" field, below). Details of the methods used in producing the Evidence Report are provided in that document.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Evidence Report produced by the Duke Evidence-based Practice Center (EPC) was reviewed during a second meeting of the Working Group in February 2002 in Chapel Hill, North Carolina. During this meeting each of the seven topics was reviewed in turn, to identify specific recommendations for the CPG. The Working Group was guided by four principles: that the recommendations be (1) evidence-based to the extent possible, (2) concise, (3) actionable, and (4) measurable. To maintain a clear connection to the scientific evidence, the Working Group assigned a grade to each recommendation based on the strength of supporting research.

In order to produce recommendations that were clinically important and clear, lack of high quality evidence for many questions compelled the Working Group to develop recommendations based primarily on expert opinion.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

Adapted from the 1996 U.S. Preventive Services Task Force.

Grade A: The panel strongly recommends that clinicians routinely provide (the service) to eligible patients. (An 'A' recommendation indicates good evidence that [the service] improves important health outcomes and that benefits substantially outweigh harms.)

Grade B: The panel recommends that clinicians routinely provide (the service) to eligible patients. (A 'B' recommendation indicates that at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.)

Grade C: The panel recommends that clinicians routinely provide (the service) to eligible patients. (A 'C' recommendation indicates that there was consensus among the panel to recommend [the service] but that the evidence that [the service] is effective is lacking, of poor quality, or conflicting or the balance of benefits and harms cannot be reliably determined from available evidence.)

Grade D: The panel recommends against clinicians routinely providing (the service). (A 'D' recommendation indicates at least fair evidence that [the service] is ineffective or that harms outweigh benefits.)

Grade I: The panel concludes that the evidence is insufficient to recommend for or against [the service]. (An 'I' recommendation indicates that evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined, and that the panel lacked a consensus to recommend it.)

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendation grades [A, B, C, D, I] are indicated after each recommendation. These definitions are repeated following the recommendations.

Anemia Recommendations

Monitoring anemia regularly

If a patient has glomerular filtration rate (GFR) $\leq$30 mL/min/1.73 m^2, then s/he should have his/her hemoglobin checked at least every three months (Grade C).

Workup of anemia

If a patient has GFR $\leq$30 mL/min/1.73 m^2 and a hemoglobin <12 g/dL if a woman, and <13 g/dL if a man, then s/he should undergo a complete work-up for anemia including iron studies (Grade B).

Treating iron deficiency

If a patient has GFR $\leq$30 mL/min/1.73 m^2 and if iron deficiency is identified, then s/he should be treated (Grade C).

Treatment with erythropoietin or erythropoietin analogue

If a patient has GFR $\leq$30 mL/min/1.73 m^2 and remains anemic despite appropriate evaluation and iron therapy, then s/he should be treated with erythropoietin or analogue (Grade B).

Monitoring blood pressure for those receiving erythropoietin or erythropoietin analogue

If a patient has GFR $\leq$30 mL/min/1.73 m^2 and is receiving erythropoietin or analogue, then s/he should have his/her blood pressure checked with each dose (Grade C).

Hypertension Recommendations

Monitoring blood pressure

If a patient has GFR $\leq$30 mL/min/1.73 m^2, then his/her blood pressure should be checked with every clinic visit (Grade A), which should be at least every three months (Grade C).

Responding to elevated blood pressure

If a patient has GFR $\leq$30 mL/min/1.73 m^2, and if blood pressure is determined to be elevated (systolic >130 mm/Hg OR diastolic >80 mmHg), then s/he should receive encouragement and instruction to initiate therapeutic lifestyle changes (Grade C) and s/he should receive intensified antihypertensive therapy (Grade B).

Treating with angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs)

If a patient has GFR $\leq$30 mL/min/1.73 m^2 and hypertension, then s/he should receive an angiotensin converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB) as a first-line agent (Grade C).

Bone Disease Recommendations

Monitoring for metabolic acidosis

If a patient has GFR $\leq$30 mL/min/1.73 m^2 then s/he should be monitored for acidosis (serum bicarbonate concentration) at least every three months (Grade C).

Correcting metabolic acidosis

If a patient has GFR $\leq$30 mL/min/1.73 m^2 then his/her chronic metabolic acidosis should be corrected to a serum bicarbonate of $\geq$22 mmol/L (Grade C).

Monitoring calcium, phosphorus, and immunoreactive parathyroid hormone (iPTH)

If a patient has GFR $\leq$30 mL/min/1.73 m^2, then s/he should have his/her serum calcium and phosphorus measured at least every three months, and immunoreactive parathyroid hormone (iPTH) levels measured at least once (Grade B) AND if calcium and/or phosphorus levels are abnormal, iPTH levels should be monitored at least every three months (Grade C).

Treating hyperparathyroidism (HPTH) and/or hyperphosphatemia

If a patient has GFR $\leq$30 mL/min/1.73 m^2, and if iPTH >100 pg/mL (or > 1.5 times the upper limit of normal for each assay used), OR serum phosphorus >4.5 mg/dL then s/he should be placed on a low phosphorus diet (<800-1000 mg/day) for one month, and phosphorus levels should be re-checked, regardless of phosphorus or iPTH levels. (Note: a low phosphorus diet implies a low protein diet). If serum phosphorus is still >4.5 mg/dL, then phosphate binder should be started (Grade B) AND iPTH levels should be monitored every three months following initiation of therapy, whether phosphorus is controlled or not (Grade B).

Managing decreased vitamin D levels (vitamin D insufficiency)

If a patient has GFR $\leq$30 mL/min/1.73 m^2 and if iPTH >100 pg/mL (or 1.5 times the upper limit of normal for each assay used), then measure 25(OH) vitamin D; AND if 25(OH) vitamin D is decreased (serum levels <30 ng/mL) then s/he should receive vitamin D_2 50,000 units orally every month for 6 months (Grade C).

Managing hypocalcemia

If a patient has GFR $\leq$30 mL/min/1.73 m^2 and corrected serum calcium is <8.5 mg/dL (using a normal reference range of 8.5-10.5 mg/dL) after phosphorus issues are addressed, then s/he should receive elemental calcium 1 g/day between meals or at bedtime (Grade C).

Treating refractory hyperparathyroidism (HPTH)

If a patient has GFR $\leq$30 mL/min/1.73 m^2 and iPTH remains >100 pg/mL (or >1.5 times the upper limit of normal for each assay used) after 3 months of previously recommended interventions, then s/he should receive oral vitamin D therapy with 0.25 mcg/day of calcitriol (Grade C) or alfacalcidol 0.25 mcg/day, to a maximum of 0.5 mcg/day.

Nutrition Recommendations

Monitoring nutritional status regularly

If a patient has glomerular filtration rate (GFR) $\leq$30 mL/min/1.73 m^2, then his/her nutritional status should be monitored by measuring body weight and serum albumin every three months (Grade B).

Managing malnutrition

If a patient has GFR $\leq$30 mL/min/1.73 m^2, and if body weight decreases unintentionally by more than 5% or serum albumin decreases by more than 0.3 g/dL or is 4.0 g/dL (for Bromo-Cresol-Green assay, or 3.7 for Bromo-Cresol-Purple assay), then s/he should be evaluated for causes. If other causes are ruled out and cause is therefore determined to be chronic kidney disease, then s/he should receive diet assessment and counseling by qualified and experienced personnel (Grade C).

Initiating renal replacement therapy (RRT) based on nutritional status

If a patient has GFR $\leq$20 mL/min/1.73 m^2, with evidence of malnutrition that does not respond to nutritional intervention in the absence of other causes of malnutrition, then s/he should begin renal replacement therapy (Grade C).

Dyslipidemia Recommendations

Monitoring for dyslipidemia

If a patient has GFR ≤30 mL/min/1.73 m^2, then s/he should be monitored for dyslipidemias; measurements should include triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and total cholesterol (Grade B).

Evaluation for secondary causes

If a patient has GFR ≤30 mL/min/1.73 m^2, and has dyslipidemia, then s/he should be evaluated for secondary causes including comorbid conditions and certain medications (Grade C).

Treatment of dyslipidemias

If a patient has GFR ≤30 mL/min/1.73 m^2, low-density lipoprotein (LDL) should be targeted to <100 mg/dL; non-high-density lipoprotein (HDL) cholesterol should be targeted to <130 mg/dL; and fasting triglycerides ≥500 mg/dL should be treated (Grade C).

Counseling and Rehabilitation Recommendations

Exercise

If a patient has GFR ≤30 mL/min/1.73 m^2 and does not engage in regular physical activity, then s/he should receive counseling and encouragement to increase physical activity. If a patient is unable to walk or unable to increase fully mobile physical activity, then s/he should be referred to physical therapy or cardiac rehabilitation (Grade B).

Evaluation, education, and encouragement

If a patient has GFR ≤30 mL/min/1.73 m^2, then s/he should receive structured education regarding preparation for RRT (Grade C).

Employment counseling

If a patient has GFR ≤30 mL/min/1.73 m^2 then s/he should be encouraged to maintain employment and be referred to vocational counseling per his/her preference (Grade C).

Timing Recommendations

Early counseling about modality of RRT

If a patient has glomerular filtration rate (GFR) ≤30 mL/min/1.73 m^2, modality of RRT should be discussed with him/her (Grade B).

GFR as a guide to RRT timing

No recommendation can be made for initiating RRT based solely on a specific level of GFR (Grade C).

Early referral for transplant evaluation

If a patient has GFR $\leq$30 mL/min/1.73 m^2 and is willing to have a renal transplant, then s/he should receive a transplant evaluation (Grade B), unless s/he has an unacceptable level of surgical risk or does not satisfy the United Network for Organ Sharing (UNOS) Ethics Committee criteria for transplant candidacy (Grade C).

Preservation of veins for vascular access

If a patient has GFR $\leq$30 mL/min/1.73 m^2 and it has been determined that s/he will receive hemodialysis, veins suitable for placement of vascular access should be preserved (Grade C).

Timing for vascular access placement

If a patient has GFR $\leq$30 mL/min/1.73 m^2, and it has been determined that s/he will receive hemodialysis, then s/he should be referred for surgery to attempt construction of a primary arteriovenous (AV) fistula (Grade C).

Definitions:

Grades of Recommendation

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CLINICAL ALGORITHM(S)

A clinical algorithm for management of bone disease for patients with advanced chronic kidney disease is provided in the original guideline document.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Lack of high quality evidence for many questions compelled the Working Group to develop recommendations based primarily on expert opinion; two-thirds of the recommendations were deemed grade C (see the "Major Recommendations" field, above). The levels of evidence supporting each recommendation are provided in the rationale following the recommendation in the original guideline document.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Anemia

Mortality and major complications during end-stage renal disease (ESRD) are associated with anemia that develops early in the course of chronic kidney disease. Correcting anemia before the initiation of renal replacement therapy may improve health outcomes.

Bone disease

- The metabolic and skeletal derangements associated with renal osteodystrophy are not easily reversed and, therefore, early interventions are important.
- It is presumed that correction of serum bicarbonate leads to prevention of bone disease and preservation of bone buffering.
- Therapy for hyperparathyroidism and/or hyperphosphatemia can prevent the progression of secondary hyperparathyroidism.
- Therapy for refractory hyperparathyroidism can improve the histologic features of renal osteodystrophy, raise bone density, and may prevent bone fractures.

Hypertension

- Patients with advanced chronic kidney disease (CKD) are at high risk for hypertension. Patients with advanced CKD who are also hypertensive usually have blood pressures elevated above recommended guidelines, even if treated with antihypertensives. In order to be treated appropriately, blood pressure must first be assessed and hypertension recognized. Lower blood pressure is an important goal in the advanced CKD patient population.
- Elevated blood pressure is clearly an important risk factor for rapid progression of kidney disease and for cardiac hypertrophy.

- Reduction in blood pressure with antihypertensive medication clearly improves measures of kidney function, slows progression to end-stage renal disease (ESRD), and improves clinical outcomes such as clinical cardiovascular events and mortality in these individuals.
- Patients receiving an angiotensin converting enzyme (ACE) inhibitor have a reduction in disease progression that is greater than for patients with similar levels of blood pressure control without ACE inhibition. The additional benefit conferred by ACE inhibitors is thought to be related, in part, to reduction in proteinuria levels. ACE inhibition has also been shown to reduce mortality and cardiovascular events in patients with pre-existing coronary artery disease and patients with diabetes mellitus and at least one other coronary artery disease risk factor. The mortality benefit conferred by ACE inhibitors may be greater for patients with elevated serum creatinine compared to those with normal renal function.
- Angiotensin II receptor blockers (ARBs) have also been shown to reduce progression of chronic kidney disease in subjects with type II diabetes mellitus.

Nutrition

Nutritional interventions are commonly advised for patients with CKD. These interventions are hoped to retard the progression of kidney disease and therefore delay the need for renal replacement therapy.

Dyslipidemias

Statins reduce coronary heart disease and all-cause mortality in the general population and should be added to the regimen of patients with advanced CKD if there is no evidence of liver disease. The lowest effective dose should be sought and serum glutamic oxaloacetic transaminase (AST) and signs of myopathy should be monitored.

Counseling and Rehabilitation

- Physical activity is an important component of health. Exercise counseling improves measures of physical functioning and work capacity in non-renally impaired persons, reduces overall mortality, and prevents deterioration in physical functioning. In patients on hemodialysis, interventions to increase physical activity have been shown to improve well-being and exercise capacity. Patients with advanced chronic kidney disease may be better able than dialysis patients to undertake increased physical activity because usually they have better functional status and less co-morbidity. Furthermore, these patients may benefit more from exercise than patients on renal replacement therapy.
- Exercise counseling studies indicated that improvements in performance-based measures of physical functioning and exercise capacity can occur without resource-intensive supervised exercise therapy. Furthermore, these studies suggest improvements in symptoms and quality of life.
- Patient education is an important component in management of advanced CKD and may be expected to influence patients' choice of and success with renal replacement modality. For example, predialysis education programs often are aimed not only at informing patients of all treatment options, but

also at decreasing anxiety for patients and their families and at providing enhanced self-care strategies.
- In general, maintaining employment is associated with better access to care through continued employer-based health insurance. Studies show that some hemodialysis patients can and do continue to work. Surveys of patients with end-stage renal disease suggest that workers have better quality of life than non-workers.

Timing of the Initiation for Renal Replacement Therapy

- It is important to properly time the initiation of renal replacement therapy in order to minimize morbidity and mortality. The role of patient factors such as therapeutic preferences is also considered especially important in timing, initiation, and choice of modality of renal replacement therapy.
- Transplantation as the first mode of renal replacement therapy results in better graft survival and decreased mortality. A study has concluded that patient survival is better for patients not dialyzed than those dialyzed, regardless of the type of kidney donor. Another study has also determined that the duration of dialysis is positively associated with the occurrence of acute rejection.

POTENTIAL HARMS

Anemia

- Severe transfusion-dependent anemia associated with anti-erythropoietin antibodies has been reported to occur rarely. Patients who are receiving erythropoietin or analogue and develop unexplained worsened anemia should be tested for these antibodies.
- Blood pressure control often deteriorates with erythropoietin therapy. Evidence suggests at least some increase in the risk of developing hypertension or of suffering an exacerbation of hypertension associated with erythropoietin therapy. Blood pressure changes are usually minimal and rarely require more than minor increases in anti-hypertensive medication.

Bone Density

- Patients receiving bicarbonate should be monitored for volume overload, although the administration of sodium bicarbonate has not induced volume overload in small controlled trials in patients with advanced CKD.
- Calcium based phosphate binders are preferred as first line agents. Some investigators advocate a maximum dose of 2 g elemental calcium/day including both dietary intake and calcium-containing binders. While this therapy may increase the risk of vascular calcification, the alternative therapies are imperfect, and therefore further limiting the dose appears premature at this time.
- Large doses of calcium based monotherapy may result in gastrointestinal intolerance and serum phosphorus levels that are resistant to lowering.
- Citrate containing compounds such as Shohl's solution or Bicitra (TM) should be avoided when using aluminum-containing compounds such as binders and antacids, since citrate therapy increases gastrointestinal absorption of aluminum and can lead to aluminum encephalopathy.

- Non-aluminum based therapy is used for chronic treatment. Aluminum based therapy should only be used for less than one month.
- Administration of non-calcium, non-aluminum based phosphate binders in this population is an off-label use and may cause acidosis in patients with advanced CKD.
- In patients receiving vitamin D, the risk of hypercalcemia may be greater when total elemental calcium intake exceeds 1.2-1.4 g/day.
- Patients with advanced CKD are at risk of adynamic bone disease if they are given excess vitamin D and become hypercalcemic. For patients with calcium >9.5 mg/dL, vitamin D use should be discontinued, the dose decreased, or the dose of calcium binder decreased.
- For patients with low immunoreactive parathyroid hormone (iPTH) levels (<40 pg/mL, or <60% of the upper limit of normal range) calcium supplements should not be given, as they may increase the risk of adynamic bone disease.
- Caution should be used when prescribing vitamin D analogues when serum calcium is in the upper range of normal, since these analogues have a low therapeutic index.

Hypertension

- There is potential for either angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) to reduce glomerular filtration rate (GFR) and hasten the progression of CKD. This may be a particular problem in patients with some degree of renal artery stenosis who are dependent on post-glomerular arteriolar constriction to maintain glomerular perfusion pressure. An acute reduction in GFR by up to 25% may occur and does not, in itself, mandate discontinuation of the medication. This acute reduction in GFR is accompanied by a reduction in glomerular sclerosis, fibrosis, and proteinuria triggered by intraglomerular hypertension.
- Blockade of angiotensin II reduces the release of aldosterone, which is an important stimulus to urinary potassium excretion. Hyperkalemia (plasma potassium above 5.1 mEq/L) occurs in approximately 10% of patients taking ACE inhibitors. The risk is higher in patients with reduced renal function. There is some evidence that in patients with GFR <60 mL/min/1.73m^2, the incidence of hyperkalemia is less with an ARB compared to ACE inhibitor. There is also limited evidence that the use of low-dose ACE inhibition may reduce the risk of hyperkalemia while still providing equivalent antiproteinuric effects. If hyperkalemia is not life-threatening, management should be attempted through dietary potassium restriction, loop and/or thiazide diuretic therapy, and transient use of a cation exchange resin.

Dyslipidemia

- The safety and efficacy of lipid lowering diet and the effects of exercise and/or weight loss in patients with chronic kidney disease are not clear.
- Combination therapies in patients with chronic kidney disease have not been examined with respect to safety and efficacy. The use of a statin with a fibrate is best avoided. Addition of bile acid sequestrants is safe in the general population and may be effective but should be avoided in patients with increased triglycerides. Nicotinic acid can be considered except in patients with liver or peptic ulcer disease or severe gout.

- Levels of bezafibrate, clofibrate, and fenofibrate are increased in patients with chronic kidney disease, while levels of gemfibrozil are not; the latter should be considered the fibrate of choice in CKD patients. All fibrates may increase serum creatinine and blood urea nitrogen (BUN) levels but not necessarily GFR.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- As with any guidelines, the recommendations in this document are not a substitute for the experience and judgment of a clinician and, as a practical matter, do not address all important management issues in detail. The Working Group acknowledges that these are not rules which require rigid conformity; as clinicians take into account individual patient needs and values, available resources and the limitations of their particular practice setting, variations in practice may be expected to occur. The objective of this document is to enhance the provider's ability to care for patients based on the best available scientific evidence.
- This guideline is not intended for use in children and adolescents. Children with advanced chronic kidney disease have unique diseases, growth and developmental changes, metabolism, neuropsychological advancements, preventive care needs, and social structures and therefore require unique approaches and therapies. While these guidelines have conceptual applicability to the comprehensive care of children with advanced chronic kidney disease, the implementation of specific strategies for the appropriate preparation of children, adolescents, and their families for renal replacement therapy requires the specialized oversight of a team with pediatric nephrology expertise. Published evidence for the management of these issues in the pediatric population is very limited.
- The clinical performance measures that have been developed on the basis of the recommendations in the clinical practice guideline are not intended for physician comparison, survey or population purposes; instead, they are meant to facilitate physician quality improvement.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Development of a clinical practice guideline and clinical practice measures are first steps in a sequence of activities aimed at improving clinical practice through formal implementation efforts. Recommended next steps include:

- Dissemination of the clinical practice guideline: In addition to providing access to this text, the clinical practice guideline should be translated into a format for quick reference.
- Production of tools for practice improvement: This includes a system for performance measurement that can be used in a variety of practice settings, as well as resources for physicians and patients to facilitate their adherence to the clinical practice guideline. Although few specific implementation tools are currently available, the original guideline document provides a review of

practice improvement tools that have been used with success in other clinical areas and hold promise for improving care of patients with advanced chronic kidney disease. These tools include:

1. Dissemination of guidelines
2. Performance feedback
3. Standing orders
4. Chart reminders
5. Patient education material
6. Personal health records
7. Computerized record reminders
8. Mailed/telephone reminders
9. Expanding access for patients in clinical settings

- Evaluation of the impact of these efforts on clinical practice and outcomes: The clinical practice measures can be used over time to examine patterns of care in response to education and distribution of practice improvement tools.
- Planned review and revision of the clinical practice guideline: It is estimated that in light of the rate of production of new evidence, the current clinical practice guideline will require updating in three to five years.

Successful guideline implementation requires proactive efforts. Previous efforts have resulted in the following conclusions:

- There is no "one size fits all" tool; no one strategy can guarantee success in all organizations. An analysis of the culture of the administration, physicians and patients--the three "players" in the implementation process--will dictate the selection of the tools.
- It is crucial to involve more than one of these essential "players" in the implementation process. An increasing emphasis on patient involvement in guideline implementation is leading the efforts in this area.
- Even for a single "player," a single strategy will not produce expected results. A multifaceted approach for each component is essential for success.

IMPLEMENTATION TOOLS

Clinical Algorithm
Quality Measures

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

RELATED NQMC MEASURES

- Renal Physicians Association Clinical Performance Measures on Appropriate Patient Preparation for Renal Replacement Therapy

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Renal Physicians Association. Appropriate patient preparation for renal replacement therapy. Rockville (MD): Renal Physicians Association; 2002 Oct. 78 p. (Renal Physicians Association Clinical Practice Guideline; no. 3). [252 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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Renal Physicians Association - Medical Specialty Society

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Appropriate Patient Preparation for Renal Replacement Therapy Working Group

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American Nephrology Nurses' Association - Professional Association
Forum of End-Stage Renal Disease Networks - Private Nonprofit Organization

GUIDELINE STATUS

This is the current release of the guideline.

It is estimated that in light of the rate of production of new evidence, the current clinical practice guideline will require updating in three to five years.

GUIDELINE AVAILABILITY

Electronic copies: Not available at this time.

Print copies: Available from the Renal Physicians Association, 4701 Randolph Rd, Suite 102, Rockville, MD 20852; e-mail, rpa@renalmd.org; telephone, (301) 468-3515; fax, (301) 468-3511.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- McCrory D, Klassen P, Rutschmann O, Coladonato J, Yancy W, Reddan D, Gray R, Owen W, Shurr E, Matchar D. Evidence report: appropriate patient preparation for renal replacement therapy. 2002 Apr. p 428.

Electronic copies available from the Renal Physicians Association (RPA) Web site.

Print copies: Available from the Renal Physicians Association, 4701 Randolph Rd, Suite 102, Rockville, MD 20852; e-mail, rpa@renalmd.org; telephone, (301) 468-3515; fax, (301) 468-3511.

PATIENT RESOURCES

None available

NGC STATUS

This summary was prepared by ECRI on May 2, 2003. The information was verified by the guideline developer on May 27, 2003.

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